I20 in adenocarcinoma without smoking (39.2±35.1%. n=6) was higher than that of adenocarcinoma with smoking (2.2±5.0%, n=10, p=0.001), and that of non-adenocarcinoma (16.9±23.6%, n=6, p=0.09). Gene mutation analysis was performed in 2 of 3 adenocarcinomas without smoking, which showed high I20 values (76.3%, 72.1%, and 63.0%). Gene mutation in EGFR was observed in these specimens. Cut-off inhibition rate of 50% appears to be suitable for the concentration of 20 μg/ml.

Conclusion: HDRA appears to be applicable to evaluate the sensitivity for gefitinib in non-small cell lung cancer. It will provide more convenient method to predict the response for EGFR-TKIs in the patients with non-small cell lung cancer, whose fresh tumor specimens are available.

P3-161 NSCLC: Molecular Targeted Therapy Posters, Wed, Sept 5 – Thurs, Sept 6

Gefitinib toxicity has been significantly correlated with survival in non-small cell lung cancer patients treated in EAP program in Czech Republic

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Background: Clinical experience with gefitinib has suggested that there are subgroups of patients with non-small-cell lung cancer (NSCLC) that demonstrate dramatic responses to this agent. Correlation between gefitinib sensitivity and adverse events in NSCLC remains controversial. Rash, the most commonly reported adverse effect of anti-EGFR therapy, has been examined as a potential marker of response and survival. Several trials evaluating anti-EGFR therapies have reported a positive correlation between rash and response and even rash and survival. In this retrospective analysis of NSCLC patients treated with gefitinib we have assessed adverse events and their relationship to treatment outcome.

Methods: 690 NSCLC patients were enrolled since January 2002 till September 2005 for the treatment with gefitinib under the EAP program in the Czech Republic. Correlations among clinicopathological characteristics, gefitinib sensitivity, and time to progression (TTP), survival and adverse events were studied.

Results: 46% of patients had no adverse event. Skin rash was the most frequent adverse event (42% any grade, G3-4: 5%), diarrhea occurred in 18% (G3-4: 2%), nausea and vomiting in 15% (G3-4: 2%) and liver toxicity in 6% (G3: 0.1%). Interstitial lung disease was not observed, pulmonary adverse events were pneumonia and bronchitis in 1.5% of patients. 27% of patients had 2 and more adverse events. Treatment was preliminary terminated due to toxicity in 10%. Skin rash was more frequent in men (44%) then in women (35%), p = 0.055, other toxicity in subgroups according to gender, stages, histopathology and pretreatment did not differ significantly. The patients with rash or diarrhea had longer time to progression (median 5.2 versus 2.7 months, p = 0.001) and survival (median 10.3 versus 5.0 months, p = 0.001) as the patients without toxicity. Rash was significantly correlated with longer survival and TTP in all subgroups according to gender and histopathology. Response rate and clinical benefit did not differ in subgroups according to toxicity.

Conclusions: In this group of 690 gefitinib treated NSCLC the expected frequency and spectrum of adverse events were observed. Most frequent toxicity was skin rash and diarrhea. Toxicity grade 3 and 4 did not exceed 5%. Patients with adverse events, particularly with the rash, had longer survival and time to progression.

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Predictive factors of efficacy and survival in Chinese non-small cell lung cancer patients treated with gefitinib

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Background: Gefitinib, a selective inhibitor of epidermal growth factor receptor (EGFR) tyrosine kinase, has been approved effective in local advanced or metastatic non-small cell lung cancer (NSCLC) previously treated with chemotherapy in Asian patients. Asian ethnicity, gender, smoking history, adenocarcinoma histology were considered associate with gefitinib response and survival. However, these predictive factors of gefitinib efficacy (response or stabilization) and survival are still unclear in Asian population.

Methods: Tumor response, survival and the clinicopathologic factors of 256 NSCLC patients treated between Sep.2002 and Mar. 2005 were collected retrospectively from the expanded access program (EAP) and multicenter registration trial of gefitinib in China. Pearson Chi-square test and Logistic regression test were performed respectively as univariate and multivariate analyses of gefitinib response. Overall survivals between groups with different predictive factors were compared by log-rank tests. Multivariate analysis was performed to identify factors that independently predict for survival.

Results: A total of 256 patients were included in this analysis. Objective response rate was 24.6% (95% confidence interval [CI]: 19.3%-29.9%) and disease control rate was 54.7% (95%CI: 48.6%-60.8%). Objective response rate was statistically significant higher in patients with younger age(≤65 years), smoking history, adenocarcinoma and longer interval from diagnosis to gefitinib treatment (≥6 months) in univariate analysis ($p<0.05$), but only younger patients(≤65 years) had statistically significant higher response rate in multivariate analysis ($p<0.05$). Disease control rate was statistically significant higher in adenocarcinoma and patients with controlled disease (CR+PR+SD) to most recent chemotherapy in multivariate analysis ($p<0.05$). The median follow-up duration was 13.1 months (range, 0.5-38.8). The median survival was 12.9 months (95% CI: 9.9-15.9) and 1-year survival was 51.8%. Significant independent predictive factors associated with longer survival in multivariate analysis were good performance status (score 0-1) and controlled disease (CR+PR+SD) to gefitinib ($p<0.05$).

Conclusions: Gefitinib is effective in local advanced or metastatic NSCLC patients in China. In Chinese NSCLC population, younger age (≤65 years), adenocarcinoma and controlled disease (CR+PR+SD) to most recent chemotherapy were predictive factors in multivariate analysis for gefitinib efficacy (response or stabilization); good performance status (score 0-1) and controlled disease (CR+PR+SD) to gefitinib were independent prognostic factors for survival.